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APPLICATION NO.	FILING DATE	FIRST NAME OF INVENTOR	ATTORNEY/AGENT	ADDRESS
09/220,142	12/23/1998	STEPHEN H. FRIEND	0301-035-0000	3800

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EXAMINER

MARSCHHEL ARDIN H

ART UNIT PAPER NUMBER

1651

DATE MAILED 06/27/2002

26

Please find below and or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/220,142

Applicant(s)

Friend et al.

Examiner

Ardin Marschel

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Apr 9, 2002
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 3-50, 58-64, 72-78, 89-100, and 105-124 is/are pending in the application.
- ~~5) ☐ Claim(s) 2, 51-57, 65-71, 79-88, and 101-104 have been cancelled ~~is/are withdrawn from consideration~~~~
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 3-50, 58-64, 72-78, 89-100, and 105-124 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on Apr 9, 2002 is/are a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- *See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☒ Interview Summary (PTO-413) Paper No(s) 23
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

Applicants' arguments, filed 4/9/02, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

NEW MATTER

Claims 18, 26, 50, 64, 96, 106, and 123 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

It is noted that claims 18, 64, 96, and 123 have been amended to now include evaluation of fractional improvement via total scatter improvement. These amendments direct the total scatter improvement as being "with respect to a cluster center in going from one cluster to two clusters". This limitation is present in instant claims 18, 64, 96, and 123, parts (a) and (d) of each claim. This scatter improvement evaluation is different from the cited written support in the specification at page 28, line 28, through page 30, line 20. Particularly, the scatter calculation must take into account that a one cluster center is different from a plurality of centers when there are two clusters

utilized in the calculation. This is accounted for in the citation on page 29, lines 13-14, wherein the total scatter is computed "with respect to the cluster centers in going from one cluster to two clusters". Thus, the above noted amendment to claims 18 etc. contains NEW MATTER in two regards. Firstly, the center (singular) versus centers (plural) contains NEW MATTER in the singular version. Secondly, the amendments add unclarity as to what center or centers is being utilized for scatter calculation. This added unclarity is also NEW MATTER. It is noted that the above NEW MATTER has also been amended into claims 26, 50, and 106, parts (a) and (d) of each claim. This rejection is necessitated by amendment.

In claim 26, last 3 lines, the phrase "the corresponding cluster" contains NEW MATTER due to the added lack of antecedent basis for "the" corresponding cluster which is indicative of a particular cluster which is not set forth previously in the claim. It also contains NEW MATTER when the cited sections of the specification in support are compared to said last 3 lines of claim 26. The closest correspondence citation for clusters has been found on page 37, lines 17-19, where the clusters or sets are associated with similar biological effects of a perturbation. This correspondence or association is not present in claim 26 which is thus broader than the written support as noted in the specification on page 37 thus supporting this NEW MATTER

rejection. This rejection is necessitated by amendment as also applied against claims 50 and 106 due to their content of the same NEW MATTER as noted in claim 26.

LACK OF ENABLEMENT

Claims 14, 22, 47, 61, 92, and 119 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is noted that the enabling discussion of the operation of *hclust* is incorporated by reference to a software package in the specification on page 24, lines 15-16. This algorithm is essential subject matter for the practice of the above listed claims and as such cannot be enabled by incorporation by reference to a printed publication. See the following paragraph regarding improper incorporation by reference for essential subject matter. It is noted that applicants have submitted documents which list *hclust* as being available but none of these submissions set forth a description of the content of this algorithm as to what is therein calculated etc. Thus, the enabling disclosure of this software has not fully set forth by which to determine what is performed thereby.

The incorporation of essential material by reference to a foreign application or foreign patent or to a publication inserted in the specification is improper. Applicant is required

to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or applicant's attorney or agent, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. *In re Hawkins*, 486 F.2d 569, 179 USPQ 157; *In re Hawkins*, 486 F.2d 579, 179 USPQ 163; *In re Hawkins*, 486 F.2d 577, 179 USPQ 167.

VAGUENESS AND INDEFINITENESS

Claims 18, 26, 50, 64, 96, 106, and 123 are rejected, as discussed below, under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 18 etc. are vague and indefinite regarding step (a) therein. In claim 18 a fractional improvement is determined but confusingly without clearly indicating what is performed in order to obtain an improvement. It is noted that steps (b)-(d) in claim 18 cites steps for obtaining an improvement. It seems that step (a) summarizes what is performed in steps (b)-(d) with the repeating step (e) but does not indicate clearly what is the actual improvement versus the improvements in steps (b)-(d) with the repeating of step (e). This is also an unclarity in the remainder of the above listed instant claims. Clarification via clearer claim wording is requested. This rejection is reiterated and maintained from the previous office action, but modified as necessitated by amendment, because of unclarity that has been

amended into the claims as summarized in the above NEW MATTER rejection.

PRIOR ART REJECTIONS:

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 1, 3-8, 10-13, 15-17, 19-21, 23-25, 27-46, 48, 49, 58-60, 62, 63, 72-78, 89-91, 93-95, 97-100, 105, 107-113, 115-118, 120-122, and 124 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Eisen et al. [PNAS 95:14863(1998) and (already of record)].

This rejection is maintained and reiterated from the previous office action, mailed 10/9/01. Applicants argue that

Eisen et al. does not suggest that some co-varying sets of genes or clusters of genes can be upregulated or downregulated by a particular collection of different drug perturbations. In response Figure 1 of the reference clearly demonstrates data wherein different perturbations are analyzed wherein serum is added at different times. Both the back serum addition and differing times for said adding back are different perturbations. The results in terms of data are displayed in columns advancing in time as noted at the top of Figure 1. Thus, applicants' arguments are non-persuasive in that they are contrary to the factual basis for the rejection. It is noted that these sets of data in Figure 1 as well as Figures 2 and 3 were previously pointed to in the previous action, mailed 10/9/01. Applicants also argue that Eisen et al. fails to suggest that sets of genes can similarly respond to a particular collection of different drug perturbations. This has already been responded to regarding said Figures 1-3 data sets in Eisen et al. and thus is a non-persuasive argument. It is noted that the additional suggestion to analyze drug treatments and drug targets such as gene sets was also set forth as a basis for this rejection in the previous office action, mailed 10/9/01. Also, since these Figures and descriptions in Eisen et al. were set forth in the previous office action and not responded to by applicants in their arguments, the arguments of applicants are not directed to the

basis for the rejection and thus moot. Applicants argue further that clustering is defined from projected cellular response profiles after the cellular constituent sets have been obtained. This argument is confusing because the sets of genes in Figures 1-3 of the reference are also clearly determined after perturbations have been applied to sets of genes from the organism under study. This argument is therefore non-persuasive as being contrary to the factual basis for this rejection. Applicants lastly argue that Eisen et al. does not suggest a step of determining the statistical significance of obtained cellular constituent sets as required in instant claims 17, 25, 49, 63, 95, and 122. In response the previous office action, mailed 10/9/01, pointed to the metrics and hierarchical clustering in the reference on page 14864 as describing clustering methods. The very first sentence in the Metrics section describes correlation coefficient use which is clearly a type of statistical significance determination contrary to the allegation of applicants. In summary, this rejection is maintained and reiterated from the previous office action, mailed 10/9/01.

Claims 1, 3-13, 15-17, 19-21, 23-25, 27-46, 48, 49, 58-60, 62, 63, 72-78, 89-91, 93-95, 97-100, 105, 107-118, 120-122, and 124 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Eisen et al. [PNAS 95:14863(1998)], taken in view of Welsh (P/N 5,686,114).

This rejection is maintained and reiterated from the previous office action, mailed 10/9/01. This rejection has been argued only by reiterating the arguments set forth against Eisen et al. These arguments have been responded to above as being non-persuasive and are equally non-persuasive regarding this rejection where the above responses are reiterated here. It is noted that Welsh does not need to suggest what is missing in Eisen et al. because the alleged missing parts in Eisen et al. have been noted above as actually being contained in Eisen et al. and, in fact, not missing.

No claim is allowed.

Applicants' amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P. § 706.07(a). Applicants are reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30


(November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703)308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (703)308-3894. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703)308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Patent Analyst, Tina Plunkett, whose telephone number is (703)305-3524 or to the Technical Center receptionist whose telephone number is (703)308-0196.

June 25, 2002


ARDIN H. MARSCHEL
PRIMARY EXAMINER